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BRISTOL, LYNN ANNE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,971	KOJIMA, TETSUO	
	Examiner	Art Unit	
	LYNN BRISTOL	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/7/08; 1/22/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 19-44 are all the pending claims for this application.

2. Claims 1-18 were cancelled and new Claims 19-44 were added in the Response of 1/7/08.

3. Applicants amendments to the claims have necessitated new grounds for rejection. This action is FINAL.

Information Disclosure Statement

4. The information disclosure statement filed 12/17/04 have been considered and entered. The examiner's initialed copy of the 1449 form from the IDS is attached.

5. The information disclosure statement of 9/15/05 for a different intended application and erroneously placed in the instant application file has been properly placed in the corresponding application.

Withdrawal of Objections

Specification

6. The objection to the specification for the improper placement of the the "Brief Description of the Drawings" is withdrawn in view of the amendments to the specification on pp. 2-3 of the Response of 1/7/08.

Withdrawal of Rejections

Claim Rejections - 35 USC § 112, second paragraph

7. The rejection of Claims 15-17 for omitting essential steps is moot for the cancelled claims.

8. The rejection of Claims 15 and 17 for the recitation “with a long linker” because the term “long” is moot for the cancelled claims.

9. The rejection of Claim 15 for the recitation “the other ends comprise a restriction enzyme site” in element b) is moot for the cancelled claim.

10. The rejection of Claim 15 in lacking antecedent basis for the limitation "the fragments obtained from the above treatment" in element d) is moot for the cancelled claim.

11. The rejection of Claim 15 in lacking antecedent basis for the limitation "the heavy and light chain variable domains against the second antigen" in element d) is moot for the cancelled claim.

12. The rejection of Claim 16 in lacking antecedent basis for the limitation "the gene" in elements a) and c) is moot for the cancelled claim.

13. The rejection of Claims 15- 17 for the recitation in elements a) and b) of Claim 15 and element a) in Claim 17 “constructing an antibody phage library in which a light chain variable domain and a heavy chain variable domain…restriction enzyme sites” is moot for the cancelled claims.

14. The rejection of Claim 17 in lacking antecedent basis for the limitation "the fragments obtained above" in element c) is moot for the cancelled claim.

15. The rejection of Claim 17 in lacking antecedent basis for the recitation “both against an antigen” is moot for the cancelled claim.

Claim Rejections - 35 USC § 103

16. The rejection of Claims 15-17 under 35 U.S.C. 103(a) as being unpatentable over McGuinness et al. (Nat. Biotech. 14:1149-1154 (1996)) and Volkel (Protein Engineering 14(10):815-823 (2001); cited in the IDS of 5/25/06) is moot for the cancelled claims.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

17. Claims 19-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims encompass a genus of linker molecules which are not supported by the original specification.

Claims 19-30 are interpreted as being drawn to methods for constructing a single chain diabody library, Claims 31-42 are interpreted as being drawn to methods for producing a construct encoding a single chain diabody library, and Claims 43 and 44 are interpreted as being drawn to a method for constructing an antibody library, where the methods require a "a linker of 30 to 150 base pairs comprising a cleavage site for a restriction enzyme", or b) a "linker of 30 to 150 base pairs comprising a cleavage site for a first restriction enzyme and a cleavage site for a second restriction enzyme that is different from, the first restriction enzyme", or c) "a linker of 30 to 150 base pairs comprising two or more cleavage sites for a restriction enzyme."

The linker molecules in addition to being required to possess these structural characteristics must also upon translation into a peptide linker allow for the proper folding of the sc diabody or scFv for antigen binding. As taught by Volker et al. (Volkel (Protein Engineering 14(10):815-823 (2001); cited in the IDS of 5/25/06):

"A scDb had a preferred length of 15 or more amino acid residues for the middle linker M and of 3-6 residues for the linkers A and B. No obvious bias towards a

preferred linker sequence was observed. Reduction of the middle linker below 13 residues led to the formation of dimeric scDb, which most likely results from interchain pairing between all the V(H) and V(L) domains. Dimeric scDb were also formed by fragments possessing a long linker M and linkers A and B of 0 or 1 residue. We assume that these dimeric scDb are formed by intrachain pairing of the central variable domains and interchain pairing of the flanking variable domains."

Therefore, the claims encompass a genus of molecules defined solely by its principal biological property, which is simply a wish to know the identity of any material with that biological property.

The specification teaches "a "linker" is not specifically limited as long as it does not interfere with expression of the antibody variable domains that are connected at both of its ends; the linker may or may not comprise restriction enzyme sites. Herein, a "long linker" means a linker of a size that enables the antibody heavy chain and light chain variable domains to be present as a scFv when the domains combined with the linker are expressed in a phage library. The length is not particularly limited, but preferably 30 bp to 150 bp, more preferably 36 bp to 90 bp, and most preferably 45 bp to 60 bp. Similarly, a "short linker" means a linker of a size that enables formation of a diabody (Db) when antibody heavy chain and light chain variable domains are combined with the linker and expressed. The length is not particularly limited, but preferably 6 bp to 27 bp, more preferably 9 bp to 21 bp, and most preferably 12 bp to 18 bp" [0058]; restriction sites are listed on p. 11, lines 8-12; and "For example, in the above case where BamHI and AccIII are used in a phage antibody library directed against antigens

A and B, a fragment may be cut out using another restriction enzyme, such as SfiI, and inserted into an appropriate vector, as shown in FIG. 1" [0059]; and "For example, when phage libraries are constructed, two BamHI sites (underlined) can be designed within the linker, as below: TABLE-US-00002 GlyGlyGlyGlySerGlyGlyGlyGlySerGlyGlyGlyGlySerGlyGlyGlyGlySer (SEQ ID NO: 3) GGTGGTGGTGGATCCGGTGGTGGTGGTTCTGGCGGCGGCGGCTCCGGAGGTGG TGGATCC (SEQ ID NO: 4)" [0080].

Accordingly, there is insufficient written description encompassing any one of the three linkers above because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics are not set forth in the specification as-filed, commensurate in scope with the claimed invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

In the absence of structural characteristics that are shared by members of the genus of a "linker" of a), b) or c); one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Enablement

18. Claims 19-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing single chain diabody libraries and constructs comprising the single chain diabody and a scFv antibody library created from a shortened linker where the VH and VL domains against any one antigen are from the same parent antibody and where the corresponding VH and VL domains are paired within the polypeptide construct, does not reasonably provide enablement for producing any of the foregoing libraries from unpaired single variable domains where the domains are from different antibodies against the same antigen or different antibodies against different antigens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence

or absence of working examples, the predictability of the art, the breadth of the claims, the quantity of experimentation which would be required in order to use the invention as claimed.

Nature of the Invention/ Skill in the Art

The claims are interpreted as being drawn to methods for producing single chain diabodies or a construct comprising a single chain diabody or scFv antibodies where the variable domains encompass a VH and a VL that are not required to be from the same parent antibody, but can be derived from different antibodies against the same antigen or from different antibodies against different antigens. The claims encompass VH and VL domains that are not necessarily paired as being from the same parent antibody.

The relative skill in the art required to practice the invention is a molecular immunologist.

Disclosure in the Specification

The specification discloses the method steps for performing the invention in Figures 1 and 2. The specification discloses one arm of the bispecific antibody may be designed to recognize one marker with the other arm recognizing a second marker (p. 7, line 23- p. 8, line 2). The specification does not enable the construction a single chain diabody or a scFv using anything but a VH and VL paired from the same parent antibody. The specification is not enabling for constructing scFv or single chain diabodies from mismatched variable domains. One skilled in the art would be required to perform undue trial and error experimentation in order to construct and screen the different libraries where VH and VL domains were from different antibodies and

recognized the same antigen, or from different antibodies that recognized different antigens. Applicants have not shown that any isolated scFv much less any diabody comprising less than a full complement of VH/VL CDRs from any parent antibody would retain the antigen binding property of the parent antibody.

Prior Art Status: CDR and Framework Requirements for Antigen Binding

In fact there are numerous publications acknowledging that the conformation of CDRs as well as FR influence binding.

MacCallum *et al.* (J. Mol. Biol. (1996) 262:732-745), analyzed many different antibodies for interactions with antigen and state that although CDR3 of the heavy and light chain dominate a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right col) and non-contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left col.).

Pascalis *et al.* The Journal of Immunology (2002) 169, 3076-3084 demonstrate that grafting of the CDRs into a human framework was performed by grafting CDR residues and maintaining framework residues that were deemed essential for preserving the structural integrity of the antigen binding site (see page 3079, right col.). Although abbreviated CDR residues were used in the constructs, some residues in all 6 CDRs were used for the constructs (see page 3080, left col.).

The fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen binding site, is underscored by Casset *et al.* (2003) BBRC 307, 198-205, which constructed a peptide mimetic of an anti-CD4 monoclonal antibody

binding site by rational design and the peptide was designed with 27 residues formed by residues from 5 CDRs (see entire document). Casset *et al.* also states that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, left col.) and this is demonstrated in this work by using all CDRs except L2 and a framework residue located just before the H3 (see page 202, left col.).

Vajdos *et al.* (2002) J. Mol. Biol. 320, 415-428, additionally state that antigen binding is primarily mediated by the CDRs more highly conserved framework segments which connect the CDRs are mainly involved in supporting the CDR loop conformations and in some cases framework residues also contact antigen (page 416, left col.).

Holm *et al* (2007) Mol. Immunol. 44: 1075-1084 describes the mapping of an anti-cytokeratin antibody where although residues in the CDR3 of the heavy chain were involved in antigen binding unexpectedly a residue in CDR2 of the light chain was also involved (abstract).

Chen *et al.* J. Mol. Bio. (1999) 293, 865-881 describe high affinity variant antibodies binding to VEGF wherein the results show that the antigen binding site is almost entirely composed of residues from heavy chain CDRs, CDR-H1, H2, H3 (page 866).

Wu *et al.* J. Mol. Biol. (1999) 294, 151-162 state that it is difficult to predict which framework residues serve a critical role in maintaining affinity and specificity due in part to the large conformational change in antibodies that accompany antigen binding (page

152 left col.) but certain residues have been identified as important for maintaining conformation.

The prior art as well as applicants own disclosure do not support that it was clearly established, that the a single variable domain alone is sufficient to define the binding specificity of an antibody, and that multiple antibodies can predictably be generated having the same binding specificity based on a single variable (or less than full complement of VH and VL CDRs).

Analyzing applicants own disclosure, the diabody embodiments have VH domains paired with corresponding VL domains. Additionally, the prior art indicate that it is the frameworks and CDRs that contribute to antigen binding. Further, there are no examples of mixing or matching of the VL domains or VH domains from different antibodies and producing an antibody that binds antigen as broadly claimed or suggested.

Prior Art Status for Single Variable Domain Antibodies

Smith-Gill et al. (J. Immunol. 139:4135-4144 (1987)) observed from chain recombination experiments that through interactions between the VH/VL pair, specificity for antigen is H chain determined, specific binding is increased when L chains of the same parental isotype are used, and that both H and L chains determine fine specificity.

Kumar et al. (J. Biol. Chem. 275:35129-35136 (2000)) discloses Fab molecules with anti-DNA (light chain) and anti-cardiolipin (heavy chain) binding activities, and that pairing of the partner chains is dependent on the particular H/L chain pairing.

Song et al. (Biochem Biophys Res Comm 268:390-394 (2000)) discloses that affinity and specificity of scFv for preS1 protein of HBV is dependent on S-S bond formation in conferring correct refolding of the fragments for retaining binding properties, and that L chains are predominant in antigen binding.

Therefore, selecting and producing just any variable domain substituted singl chain diabody or scFv with the ability to properly associate and assemble into a fully functional antibody which maintains the binding specificity for the original antigen would be highly unpredictable based on the methods described in the specification and the prior art disclosures.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. Claims 19-22, 31-34, 43 and 44 are under 35 U.S.C. 103(a) as being unpatentable over McGuinness et al. (Nat. Biotech. 14:1149-1154 (1996); cited in the PTO 892 form of 8/8/07) and Volkel (Protein Engineering 14(10):815-823 (2001); cited in the IDS of 5/25/06).

The interpretation of the claims is discussed above.

The claims were prima facie obvious at the time of the invention in view of McGuinness and Volkel.

McGuinness discloses methods for constructing an antibody phage display library where the V regions from antibodies against the hapten phOX or Dig are constructed into two pools of scFvs repertoires having a 15-amino acid linker between each VH and VL domain, where the orientation of the domains is VH-linker-VL (p. 1150, Col. 1, ¶1). The scFv pools were recombined into a diabody format: VHA-VLB-rbs (linker)-VHB-VLA, where the linker between each VH and VL domain was "shortened" to a zero linker (p. 1150, Col. 2, ¶1) using one of two methods: ligation mediated assembly or cassette cloning where the final diabody is inserted into an expression vector.

For ligation-mediated assembly, a two- (Fig 21, A-C) or three-step (Fig. 2iD) process is taught in the Materials and Methods on p. 1153, ¶2. In the three-step approach, an 800 bp fragment comprising Dig VH-phOxVL and phOxVH fragment are cut with a restriction enzyme and ligated, then the ligated fragment was mixed with a Dig VL fragment and digested with another restriction enzyme, and then ligated to produce the diabody insert. The two-step approach comprised taking the 800 bp

fragment comprising Dig VH-phOxVL and phOxVH and a phOxVH-DigVL fragment, ligating the mixture and digesting with restriction enzymes to produced the diabody insert.

For cassette cloning, VHA-VLB and VHB-VLA fragments were generated by PCR extension from the scFv pools, and the fragments digested with different restriction enzymes (Fig. 2ii) to produce a DigVH-phOxVL fragment and a phOxVH-DigVL fragment with terminal restriction sites followed by assembly into the diabody (p. 1151, Col. 1, ¶2; and M & M, p. 1153, Col. 2, ¶2).

The 15 amino acid linker of McGuinness is considered as reading on the linker for the first and second single scFvs and the HV and LV. The claims are not drawn to the specific order in which the VH1 and VL1 or the VH2 and VL2 should occur. In other words, McGuinness teaches a diabody format: VHA-VLB-rbs (linker)-VHB-VLA which reads on the instant claims

Volkel discloses constructing a diabody phage display library comprising single chain diabody CEA scFv/Gal scFv with a randomized middle linker from where the M linker is of variable length and comprises at least one restriction site (See Figure 2A and B). Volkel discloses generating a fragment comprising GalVL-M linker- GALVH where the M linker comprises a restriction site and subcloning the fragment into the linker region for the CEA scFv where the linker region comprises two restriction enzyme sites, BstE II and Sac I. Volkel discloses generating clones with variable linker and M-linker lengths and comprising different amino acid sequences (Tables III and IV) which are cloned into an expression vector.

One skilled in the art would have been motivated and been assured of reasonable success in having produced the instant methods at the time of the invention based on the combined disclosures of McGuinness and Volkel because each disclose the technology for constructing single-chain diabody phage display libraries where a scFv recognizing a first antigen comprising a linker with a restriction enzyme site and a second scFv recognizing a second antigen comprising a linker are treated with a restriction enzyme in order to obtain fragments which are then ligated in order to construct a final fragment having the VH and VL domains against the second antigen inserted between the VH and VL domains against the first antigen are assembled into the diabody phage display library. Each of the references discloses techniques involving differential restriction enzyme digestion of various fragments and the technology for selective insertion of the VH2/VL2 or VL2/VH2 pair between the VH1/VL1 or VL1/VH1 domains to generate a phage display diabody library. Each of the references teaches obtaining fragments comprising variable domains and shortening the linker between the domains in a ligation (PCR extension step). Based on the combined reference disclosures, one skilled in the art could have been assured of success in introducing linkers between VH and VL domains comprising restriction sites for subcloning into or between VH and VL domains against a different antigen because the references taught that subfragments could readily be generated and where a VH/VL pair against one antigen was inserted between the VH and VL against a different antigen. McGuinness teaches that construction and selection from such a library is possible and it avoids unfavorable combinations (p. 1153, Col. 1, ¶2), and Volkel discloses generating single-

chain diabodies with optimized linker sequences and expressed by phage display where correctly folded molecules can be screened against a variety of different target cells and antigens (p. 822, Col. 2, ¶3). Further, one skilled in the art could have readily constructed a self-ligating antibody library based on the method steps of McGuinness and Volkel to produce a second library having a shorter linker in relying on restriction enzyme sites in linker to restrict out a certain length of the linker to obtain a shorter linker.

For all of the foregoing reasons, the claimed method at the time of the invention was prima facie obvious to one of ordinary skill in the art over the combined reference disclosures of McGuinness and Volkel.

Conclusion

20. No claims are allowed.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

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